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# Patient education program to enhance decision autonomy in multiple sclerosis relapse management: a randomized-controlled trial

S Köpke<sup>1</sup>, J Kasper<sup>1</sup>, I Mühlhauser<sup>1</sup>, M Nübling<sup>2</sup> and C Heesen<sup>3</sup>

**Background** Contrary to strong recommendations for high-dose intravenous corticosteroid treatment for relapses in multiple sclerosis (MS), uncertainty remains about most aspects of relapse management. Oral corticosteroids administered by physicians or patients themselves or no corticosteroids also appear justifiable.

**Objective** To evaluate an education program that aims to involve patients with MS in decisions on relapse management.

**Methods** In three German MS centers, 150 patients with relapsing MS were randomly assigned to a single, 4-h group session or a standard information leaflet. The primary outcome measure was the proportion of relapses with oral or no corticosteroid therapy as an indicator of patient autonomy in treatment decision making. Other outcomes included perceived decision autonomy, quality of life, and disability status.

**Results** In the intervention group (IG), 108/139 (78%) relapses were treated with oral or no corticosteroids compared with 101/179 (56%) in the control group;  $P < 0.0001$ . Patients' perceived autonomy of treatment decision making was significantly higher in the IG;  $P < 0.0001$ . Quality of life, disability status, and adverse events of corticosteroid therapies were comparable.

**Conclusion** The patient education program led to more autonomous decision making in patients with relapsing MS. Relevant changes in relapse management were observed. *Multiple Sclerosis* 2009; 15: 96–104. <http://msj.sagepub.com>

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**Key words:** decision making; decision support technique; glucocorticoids; multiple sclerosis; patient education; patient participation

## Introduction

Multiple sclerosis (MS) is characterized by many uncertainties. Course and prognosis are variable and difficult to predict. MS commonly starts with a relapsing–remitting course. Relapses vary considerably [1]. Often, doubts remain about individual relapse diagnosis [2]. However, relapses are poor predictors of long-term prognosis [3–5].

High dose intravenous (i.v.) methylprednisolone is widely recommended as standard relapse treatment, although recommendations [6–8] and prescription practices are inconsistent [9]. Overall,

evidence for the effectiveness of corticosteroid therapy (CC) for MS relapses is sparse. There certainly is a need for high-quality studies to facilitate informed decision making. CC may improve short-term functional recovery but not long-term disability or prognosis [4,10]. Adverse effects are frequent and potentially harmful [10,11]. Preferable route, dosage, and duration of CC remain unclear [10,11]. Oral and i.v. administration appear comparable in efficacy [12], but experts nevertheless favor a “hit hard and early” approach of i.v. high-dose CC [7].

Adherence to this recommendation may elicit substantial distress in patients, particularly when

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<sup>1</sup>Unit of Health Sciences and Education, University of Hamburg, Hamburg, Germany

<sup>2</sup>GEB, Gesellschaft für Empirische Beratung mbH, Denzlingen, Germany

<sup>3</sup>Institute for Neuroimmunology and Clinical MS Research (INiMS), University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Correspondence to: Sascha Köpke, Unit of Health Sciences and Education, University of Hamburg, Martin-Luther-King-Platz 6, D- 20146 Hamburg, Germany. Email: [sascha.koepke@uni-hamburg.de](mailto:sascha.koepke@uni-hamburg.de)

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the relapse starts on a weekend or during a holiday or when treatment interferes with personal life planning [13]. The discrepancy between the weak evidence on i.v. high-dose CC and the possible negative implications for patients urges patient involvement in the decision [11,14].

Patients must be given the opportunity to get involved in making decisions about their health care. Increasing patients' autonomy in treatment decision making has been claimed to be an ethical imperative, which is reflected by the principle of informed choice [15]. Patients with MS opt for active roles in treatment decisions [8,16] and report substantial unmet information needs [17]. This encourages patient involvement in disease management and informed decision making by providing evidence-based decision aids and self management opportunities [8].

We report the effects of a patient education program that involves patients with MS in decision making about relapse therapy.

## Patients and methods

### Participants

Participants were recruited by advertisements in local newspapers in Hamburg, the national MS self-help-group journal, and directly from the three study centers in Germany: two MS clinics located at a University Hospital (Hamburg) and a General Hospital (Osnabrück), respectively, and one neurologist's practice (Herborn). Patients were eligible if they reported a physician-confirmed diagnosis of MS with at least one relapse during the past 12 months or at least two relapses during the past 24 months, had no major cognitive deficit, and were aged 18 or more. We excluded patients with a history of steroid sensitivity and/or pregnancy.

We recruited participants between May 2003 and June 2004. A total of 240 patients sought information about the study. After brief information about the study, 221 were interested in participating, of which 150 were eligible and agreed to participate (Figure 1). All participants gave written informed consent and were randomized to one of two groups. The study was approved by the ethics committee of the Hamburg Chamber of Physicians.

### Procedures

The study was a randomized controlled trial with a follow-up period of 2 years. We used computer-generated randomization lists for concealed allocation of participants by external central telephone. Participants were stratified by study center and

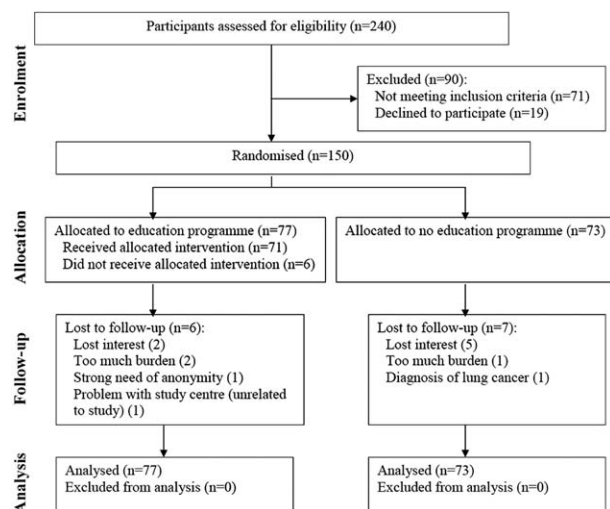


Figure 1 Flow of participants through trial.

drawn consecutively using three separate randomization lists. Participants could not be blinded as they knew if they received the program or not. In addition, for practical reasons educators and assessors were not blind to participants' allocation. To minimize bias, assessment was carried out using standardized questionnaires. One author (SK) supervised assessors regularly.

Participants in the intervention group (IG) took part in a structured 4-h education program on relapse management in MS (Table 1). Ten participants with their partners or close relatives, who might regularly be involved in treatment decision making, were invited per session. Two weeks before the session, participants received a 40-page educational booklet summarizing the evidence on relapses and relapse management, based on the principles of evidence-based patient information [18]. For example, pictograms of human stick figures were used to illustrate treatment effects. Two educators held the program: a nurse and a specially trained patient with MS. At one center (Herborn), the MS-practice nurse carried out the training. The program was based on the protection motivation model [19] applied to decisional autonomy. The "Protection Motivation Theory" [19] describes coping with a health threat as a result of two appraisal processes addressing the threat perception and the individual coping concept, in which the behavioral options to tackle the threat are addressed [20]. The appraisal leads to the intention to perform adaptive responses (protection motivation). The model has been widely used to predict and communicate health behaviors [20].

To increase treatment choices and enable more treatment autonomy, participants were offered a prescription of 30 tablets of 100 mg methylprednisolone, allowing for a 3-day course of high-dose CC

**Table 1** Structure and content of the patient education program on MS relapse management

Part	Duration (minutes)	Topic	Contents/materials
1	45	Personal experiences	Introduction round focusing on patients and relatives experiences with relapses and relapse management
2	30	Relapses	PowerPoint presentation
3	60	Relapse therapy	PowerPoint presentation, education booklet, posters with internet recommendations for corticoid therapy, group work, patients' presentations on pros and cons of recommendations
4	15	Oral CC therapy	PowerPoint presentation, information sheet on oral corticoid therapy (incl. possible serious adverse effects)
5	30	Options	decision tree/management algorithm (poster and work sheets), individual work on past and future relapse management, patients' presentations
6	45	Reflection	Guided discussion focusing on uncertainty and management of uncertainty connected to relapse management, catalyzing of individual goals, "take home question"
7	15	Evaluation	Evaluation sheets

(1 g/day). Prescriptions were prepared in advance by the cooperating neurologists at the study centers and given to participants after the program if requested. The curriculum was based on the practical oriented approach as described by Meyer [21], for example, participants had to "advertise" different treatment recommendations prepared in small-group sessions or were asked to reflect on personal management strategies using worksheets (Table 1). The detailed curriculum together with an in-depth description and discussion of the underlying theoretical model was part of a thesis work [22] and will be published separately. After the educational program, treating physicians of participants were sent a fax informing them about their patients' inclusion in the study together with brief study information. For ethical reasons, also participants in the control group (CG) had to be informed about all available treatment options. Therefore, they received a 2-page standard information leaflet on relapse treatment including the option of oral CC therapy.

We assumed that the program would increase decision autonomy. As an indicator for this, we chose as primary endpoint the proportion of relapses with oral CC therapy or without CC therapy within 2 years of follow-up. Secondary endpoints were time to initiation of CC treatment, location and invasiveness of CC treatment and costs. We also assessed perceived decision autonomy, quality of life, and disability status.

Outcome evaluations followed a pre-defined assessment protocol using standardized evaluation sheets. Baseline data on participants' characteristics were assessed by telephone before allocation to treatment groups.

### Relapses and relapse management

Participants were contacted by telephone every 12 weeks by the study center using a standardized

protocol. Participants were asked to report relapses and relapse therapy. We further asked for details of relapse symptoms, relapse course, perceived autonomy of treatment decision, adverse events of CC treatment, and MS-related telephone or personal contacts with physicians. At the end of the study, two neurologists, who were blinded to participants' allocation, independently rated relapses from case report files. Differing ratings were solved by consensus.

### Location and invasiveness of CC treatment

Location and invasiveness of CC therapy were used as a further indicator of decision autonomy. Non-medication was considered the least invasive, followed by oral CC therapy, i.v. outpatient, and i.v. inpatient therapy as the most invasive "location" of treatment. Combined oral and i.v. CC treatment was rated as i.v. and oral CC therapy included low-dose oral treatment regimes.

### Perceived decision autonomy

For each treatment decision, participants were asked a single question about their perceived role in the decision process and their grade of satisfaction with this role [23].

### Negative side effects of the program

Apart from adverse events of CC treatment, we aimed to evaluate possible negative side effect of the intervention by comparing participants' changes in quality of life and disability status over 2 years.

### Quality of life

Participants' quality of life was measured with the German version of the "Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS)." This validated questionnaire assesses disease-specific quality of life with five subscales: communication, mood, upper limb mobility, lower limb mobility, and fatigue. Subscale and total scores range from one to five, high scores indicating low quality of life [24]. The questionnaire was sent to the participants and filled in directly after randomization and at the end of follow-up.

### Disability status

Participants' functional status was assessed with the UK Neurological Disability Scale (UNDS) [25], a questionnaire-based measure of disability in MS. The German version has recently been validated [26]. The original version comprises 12 categories (each scoring 0–5) with a total score ranging from 0 to 60 (0 = no disability). For practical reasons we omitted the category on sexuality, leading to a maximum score of 55. Scores were obtained by telephone before randomization and at the end of follow-up.

### Self-rated disease course

During the final telephone interview, we asked participants if they rated their disease condition as improved, unchanged, or worse compared with their condition at the beginning of the study.

### Costs

An economic evaluation was a pre-planned secondary endpoint and will be published separately.

### Statistical analysis

We calculated sample size on the basis of the primary outcome measure (proportion of relapses with oral CC or without CC therapy). We assumed that all participants would experience at least one relapse during the study period, that there would be a mean rate of two relapses over 2 years, that there would be 30% relapses with oral or no CC medication in the CG, and that we could achieve a clinically relevant increase to 50% in the IG. Therefore, 67 participants per group were needed (90% power, 5% two sided significance level). With a dropout rate of 10%, 74 participants per

group were needed. No interim analysis was carried out, no stopping rules applied.

All statistical analyses were carried out using SPSS for Windows Release 12. The external statistician (MN) was kept blinded to participants' allocation. We used descriptive statistics to outline the characteristics of the trial participants. Primary comparisons assessed the effects of the intervention over 2 years on an intention to treat basis. According to the original protocol, treatment of relapses was chosen as the analysis level rather than persons. Because participants had different relapse rates, the postulated independency of single observations may be violated. To control for this possible bias, we conducted a supplementary analysis using data aggregated on persons' level. In addition, a per protocol analysis was carried out. For analysis with nominal data, Pearson's Chi-squared test was performed, for the comparison of means in metrical data analysis of variance (ANOVA) and unpaired *t*-tests were applied. When normality did not hold, Mann-Whitney *U*-tests were used. Confidence intervals for differences in proportions were calculated using the method recommended by Newcombe [27]. We considered results to be statistically significant if the two-tailed *P* values were less than 0.05.

The trial is registered with Current Controlled Trials (ISRCTN73885145).

## Results

### Participant flow and follow-up

In total, 240 patients were assessed for eligibility to take part in the study. Of these, 150 were randomized. Thirteen participants terminated the study early, six in the IG, and seven in the CG, mostly because they lost interest or felt burdened by the study participation (Figure 1). Baseline demographics were comparable between groups (Tables 2 and 3).

In both groups, all but one participant had previous experience with CC therapies, the majority (79% and 81%) rating relapse therapy with CC as effective. Previous relapse therapies were comparable between groups on patient and relapse level and reflect common practice [9].

### Relapses and relapse management

Participants reported 318 relapses over 2 years of follow-up. More relapses were reported in the CG than in the IG group (179 vs 139). The proportions of relapses verified by neurologists were similar for both groups: 95 (68%), IG vs 124 (69%), CG.

**Table 2** Baseline characteristics of participants

	Group <sup>a</sup>	
	Intervention (n = 77)	Control (n = 73)
Mean (SD) age (years)	37.3 (7.2)	38.8 (8.1)
Female	63 (82)	53 (73)
Married	37 (48)	35 (48)
12 or more years of education	38 (49)	42 (58)
RRMS	72 (94)	67 (92)
Mean (SD) years since diagnosis	4.9 (5.1)	5.5 (4.9)
Mean (SD) number of relapses in the last 2 years	3.1 (2.1)	3.2 (2.5)
Participants with at least one CC therapy	74 (99)	72 (99)
Participants rating CC therapy as effective	61 (79)	59 (81)
Mean (SD) physician contacts in the last year	9.3 (8.1)	10.3 (9.2)
Participants with current immunotherapy	55 (71)	48 (66)
Mean (SD) HAQUAMS (total score)	4.0 (0.6)	3.9 (0.7)
Mean (SD) UNDS (abridged version)	7.2 (5.9)	8.6 (6.4)

Values are numbers (percentages) unless stated otherwise.

RRMS, relapsing–remitting multiple sclerosis; CC, glucocorticoids; HAQUAMS, Hamburg Quality of Life Questionnaire in Multiple Sclerosis; UNDS, United Kingdom Neurological Disability Scale.

<sup>a</sup> No statistically significant differences between groups ( $P$  values > 0.05).

Relapse management differed significantly between groups. In the IG, more relapses were treated with oral CC or without CC therapy: difference = 22%; 95% CI 11–31%; number needed to treat (NNT) 5. The effect was comparable in the per protocol analysis: difference = 23%; 9–29%; NNT 4; and for verified relapses: 65 (68%), IG vs 56 (45%), CG. Participants in the IG were more likely to choose less invasive treatment options ( $P = 0.001$ ). More participants in the IG reported relapses with a perceived active role in treatment decision making (difference = 27%, 16–37%) (Table 4). Relapses were chosen as unit of analysis. To control for a possible dependency between participants and treatment form, a similar analysis was conducted on the participants' level (Table 5). Here, participants in the IG were also more likely to choose less invasive treatment options, although the results did not reach statistical significance (Table 5).

Satisfaction with the decision process was high with no differences between groups. The proportion of severe relapses was comparable between groups. In the CG, severe relapses were more often treated

with CC (difference = 37%, 20–53%). There were no differences in reported adverse effects of CC therapy. Participants in the IG reported fewer telephone calls to physicians (mean difference = 3.3, 0.1–6.5). As the data for visits to physicians was not normally distributed, a Mann–Whitney test for means was performed, showing a significant difference (difference in medians = 6,  $P = 0.03$ ) (Table 4).

#### Adverse effects related to CC therapy

Patient-reported minor adverse effects related to CC therapies were comparable between groups. Severe adverse effects were not reported (Table 4).

#### Quality of life and disability status

We found no differences in changes of health-related quality of life or disability status between groups, suggesting that the program has no negative side effect (Table 6).

**Table 3** Self-reported relapse therapy in the 24 months before study

	Patients <sup>a</sup>		Relapses <sup>b</sup>	
	Intervention (n = 77)	Control (n = 73)	Intervention (n = 237)	Control (n = 232)
No CC therapy	5 (6)	4 (5)	46 (19)	38 (16)
CC therapy	72 (94)	71 (97)	191 (81)	194 (84)
Outpatient i.v.-CC therapy	47 (61)	45 (62)	111 (47)	112 (48)
Inpatient i.v.-CC therapy	35 (45)	35 (48)	53 (22)	62 (27)
Oral CC therapy	19 (25)	20 (27)	32 (14)	25 (11)

CC, glucocorticoids.

Values are numbers of patients or relapses (percentages).

<sup>a</sup>Sums exceed patient numbers as some patients had different treatments.

<sup>b</sup>More therapies than relapses, as some were combined CC therapy regimes.

**Table 4** Outcome variables: relapses

Outcome measure	Intervention (n = 77)	Control (n = 73)	Difference in proportions unless marked <sup>a</sup> (95% CI)	P value
<b>Relapses</b>				
Relapses	139	179		
Participants with at least one relapse	55 (71)	58 (79)	-8 (-21 to 6)	0.2
Mean (SD) number of relapses per participant	1,9 (1,6)	2,7 (2,1)	-0.8 (-1.4 to -0.1) <sup>a</sup>	0.017
<b>CC Therapy</b>				
Relapses with oral or without CC therapy (ITT)	108 (78)	101 (56)	22 (11 to 31)	<0.0001
Relapses with oral or without CC therapy (PPA)	105 (79)	101 (56)	23 (9 to 29)	<0.0001
Relapses without CC therapy	78 (56)	73 (41)	15 (4 to 26)	(0.001)
Relapses with oral CC therapy	30 (22)	28 (16)	6 (-3 to 15)	
Relapses with outpatient i.v.-CC therapy	29 (21)	66 (37)	-16 (-25 to -6)	
Relapses with inpatient i.v.-CC therapy	2 (1)	12 (7)	-6 (-10 to -1)	
<b>Management</b>				
Relapses with active role in treatment decision <sup>b</sup>	93 (69)	74 (42)	27 (16 to 37)	<0.0001
Relapses with satisfactory decision making process <sup>c</sup>	122 (88)	162 (91)	4 (-1 to 10)	0.29
<b>Other</b>				
Severe relapses <sup>d</sup>	49 (35)	68 (38)	-3 (-13 to 8)	0.62
Severe relapses with CC therapy <sup>d</sup>	23 (47)	57 (84)	-37 (-53 to -27)	<0.0001
Reported adverse effects of CC therapy	5 (4)	13 (7)	-3 (-9 to 2)	0.44
Median (range) number of visits to physicians	13 (0 to 236)	19 (0 to 75)	-6 (n/a) <sup>a</sup>	0.03 <sup>e</sup>
Mean (SD) number of telephone calls to physicians	9.1 (8.8)	12.4 (10.3)	-3.3 (-0.1 to -6.5) <sup>a</sup>	0.04

Values are numbers (percentages) unless stated otherwise.

CC, glucocorticoids; ITT, intention-to-treat analysis; PPA, per-protocol analysis.

<sup>a</sup>Differences in means or medians.

<sup>b</sup>N = 312.

<sup>c</sup>N = 301.

<sup>d</sup>Relapses where defined as severe, when patients reported severe worsening in either gait, balance or vision, or sensory or bladder symptoms and/or new symptoms affecting at least two of these functional systems.

<sup>e</sup>Mann-Whitney U-test.

### Self-rated disease course

Participants in the IG rated their course of disease significantly better than participants in the CG ( $P = 0.027$ ) (Table 6).

## Discussion

This is the first study that evaluates an evidence-based decision aid by means of a patient education program addressing an important field of decision making in MS. The intervention had substantial impact on relapse management and decision mak-

ing. Physician-controlled therapies were reduced, and participants were more likely to refrain from CC therapy. Decision autonomy was promoted.

The number of relapses reported was considerably higher in the CG. As the groups were comparable at baseline, this might be regarded as an intervention effect. Definition and description of relapses was an important part of the program rendering participants in the IG more capable to differentiate fluctuations ("pseudo-relapses") that do not warrant intervention. Furthermore, it cannot be ruled out that the increased sense of control might have positively affected psychologically triggered mechanisms of relapses [28].

**Table 5** Relapse therapies per participant

	Intervention (n = 77)	Control (n = 73)	Difference in proportions (95% CI)	P value
Participants with at least one relapse	55 (71)	58 (79)	-8 (-21 to 6)	0.2
Participants with untreated relapses	41 (75)	35 (60)	15 (-3 to 31)	0.08
Participants with relapses treated with oral CC therapy	16 (29)	16 (28)	1 (-15 to 18)	0.86
Participants with relapses treated with outpatient i.v.-CC therapy	20 (36)	27 (47)	-11 (-28 to 8)	0.31
Participants with relapses treated with inpatient i.v.-CC therapy	2 (4)	10 (17)	-13 (-24 to 3)	0.21

Values are numbers (percentages).

CC, glucocorticoids.

**Table 6** Outcome variables: quality of life, disability status, disease course between-group differences in means (SD) unless stated otherwise between baseline and 2-year follow-up

	Intervention (n = 77)	Control (n = 73)	Difference (95% CI)	P value
Health-related quality of life (HAQUAMS)	n = 70	n = 66		
Total	0.5 (0.4)	0.2 (0.4)	0.3 <sup>a</sup> (-17.1 to 11.6)	0.17
Disability status (UNDS)	n = 71	n = 66		
Total	-0.9 (4.1)	0.6 (4.8)	-1.5 <sup>a</sup> (-6.5 to 0.9)	0.29
Participants' self-rated disease course, numbers (%)	n = 71	n = 66	Difference <sup>b</sup> (95% CI)	
Better	10 (14)	10 (15)	-1 <sup>b</sup> (-13 to 11)	(0.027)
Unchanged	38 (54)	21 (32)	22 <sup>b</sup> (5 to 37)	
Worse	23 (32)	35 (53)	-21 <sup>b</sup> (-36 to -4)	

HAQUAMS, Hamburg Quality of Life Questionnaire in Multiple Sclerosis; UNDS, United Kingdom Neurological Disability Scale.

<sup>a</sup>Differences in means.

<sup>b</sup>Differences in proportions.

The number of relapses with oral CC therapy or no therapy in the CG was higher than expected and noticeably higher than before randomization. This is most likely a study effect. Participants who decided to participate were highly motivated and willing to reconsider usual treatment practice.

The follow-up period of 2 years does not allow conclusions about long-term effects on disease course. However, we consider negative long-term effects unlikely for the following reasons. First, the program did not lead patients to abandon relapse treatment, but rather use it more cautiously. Participants in the IG may have decided more carefully and consciously. Second, recent studies have shown that relapse frequency or severity do not predict long-term disease progression [3–5], further questioning the need of consequent relapse treatment.

There has been concern that evidence-based patient information might increase anxiety and emotional distress [13]. However, in pre-studies with patients with MS, we have found no adverse emotional effects of this kind of information [13], which was reproduced in this study. We also found no differences between groups for quality of life and disability status, whereas clinical global impression of participants in the IG indicated a better disease course after 2 years. As a limitation, we neither can conclude on intermediate health status nor on long-term consequences of altered management concept. Severe relapses were equally distributed between groups. Similar to overall relapse treatment, in the IG less relapses categorized as 'severe' were treated with CC. This can be interpreted as further evidence for increased patient autonomy in the IG as a result of the intervention. As there is no sound scientific evidence that participants with more severe symptoms particularly benefit from CC therapy, the high rate of CC therapies in the CG might rather indicate decisions based on physicians opinions and not informed decision making.

Participants in the IG were offered a prescription of CC tablets as part of the educational program. It

could be argued that this was the intervention's main mode of action. However, the prescription might have been only of minor influence, as the program not only led to more oral CC therapies but also predominantly increased the number of relapses without CC therapy and led to enhanced decision autonomy. Still, the availability of the prescription might have added to the intervention effect. In addition, it has been stated that decision aids and patient education programs are complex interventions, consisting of various components that cannot always be sufficiently identified [29] and can therefore not be evaluated separately [30].

An important strength of this study is the choice of the primary outcome measure that was chosen based on the results of previous studies. So far, studies evaluating decision aids have rarely shown relevant change in health behavior [31]. Furthermore, answering patterns on questionnaires might not adequately reflect actual roles in the decision making process because they are highly influenced by social desirability and self concepts [32]. Thus, we chose a more robust indicator of decision autonomy. The main outcome measure combines two important requirements for the evaluation of decision aids. It reports the program's effect on participants' preferences [31] and at the same time strongly indicates that decision autonomy could be realized. The results are impressive if one considers the strong recommendations for high dose i.v. CC therapy in Germany. On the contrary, the weak evidence on MS relapse therapy also justifies alternative treatment regimes or no CC treatment. In view of the strong recommendations for i.v. high-dose CC therapy, we considered any sensible alternative treatment option (i.e., oral or no CC therapy) as an indicator for increased decision autonomy. Therefore, the primary outcome measure seems an appropriate and valid indicator of patient autonomy in treatment decision making. The fact that satisfaction with decision making was high and comparable in both groups further

supports the choice of our primary outcome measure. There are further strengths of this study. Evaluation of outcome measures was carried out in short intervals through personal contact, and follow-up covered a relevant period of time with a low dropout rate of less than 10%. As we aimed to reflect common practice, patients were recruited by media advertisements and not solely through specialized centers. Informed decision making requires the evidence to speak for itself rather than the expert explain the evidence. Accordingly, educators were not physicians or other acclaimed experts but specially trained nurses and patients with MS. In addition, this allows the program to be easily transferred to other practice centers using a train-the-trainer program.

There are factors limiting the study results. First, for practical reasons, outcome assessors were not blinded to participants' allocation, which might have introduced a bias favoring the IG. Because the assessment followed a standardized questionnaire and assessors were frequently supervised, results are still likely to be valid. Furthermore, the neurologists who rated the relapses and the external statistician were kept blinded to participants' allocation. Second, we were not able to evaluate time between relapse start and treatment initiation as a further indicator for decision autonomy. However, all other outcome data show consistent evidence for enhanced decision autonomy. Third, there were no clinical visits for medical relapse assessment, as these might have interfered with the study goals of increased patient autonomy. As a result, we are not able to finally assess the accuracy of participants' reports of relapses, making variation in the accuracy of relapse reporting between groups possible. Still, considering the uncertainties in physicians diagnosing a relapse [2], asking participants appears a valid and patient-centered method to assess relapse frequency. In addition, the blinded neurologists' ratings show comparable rates of verified relapses between groups. In accordance with aims and definition of decision aids to increase patients' decision autonomy [33], we have targeted patients and not physicians. Therefore, we are not able to judge on the role of treating physicians in the decision process. In addition, we had no systematic information on physicians' attitudes about the aim of the study. Nevertheless, an ongoing implementation study of the program in German rehabilitation centers shows high acceptance by physicians for adapted versions of the program, for example, without prescriptions provided to participants and/or with a follow-up "question and answer" discussion group with a neurologist. These modifications that do not interfere with the major aim of communicating evidence and uncer-

tainties might add to the program's transferability to other settings.

The program represents an innovative design of a patient decision aid. It uses a different strategy compared with most previously developed decision aids [33]. It must not be confused with a self-management program. Such programs usually provide participants with clear strategies to achieve outcomes desired by health care providers [34]. On the contrary, the program is consistent with current definitions of decision aids because it aims to facilitate informed decision making by, among other aspects, presenting treatment options, helping to appreciate scientific uncertainties and identifying personal values in the decision process [33].

There are advantages inherent in the present concept of choosing a patient education program as patient decision aid. It allows participants to share and compare personal experiences on relapse management and discuss the information provided.

In addition, the study results again highlight the need for high-quality randomized controlled trials evaluating the effectiveness of different CC treatment regimen using patient relevant outcome measures [11].

In conclusion, we found that the evidence-based patient education program facilitated decision autonomy. Desirable outcomes for patients and most likely for the health care system were shown. The program should be made available as part of routine MS care.

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**Contributors:** IM and CH initiated the study. SK, JK, IM, and CH wrote the study protocol. SK developed the program and coordinated the study, data collection, analysis, and interpretation. SK and CH wrote the educational booklet. SK wrote the paper, JK calculated the sample size. JK and MN designed and performed statistical analyses. SK, JK, IM, and CH are guarantors. All authors commented on drafts and have seen and approved the final version of the paper.

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## References

- Weinshenker, BG, Bass, B, Rice, GP, *et al.* The natural history of multiple sclerosis: a geographically based study. 2. Predictive value of the early clinical course. *Brain* 1989; **112**: 1419–1428.
- Liu, C, Blumhardt, LD. Assessing relapses in treatment trials of relapsing and remitting multiple sclerosis: can we do better. *Mult Scler* 1999; **5**: 22–28.
- Richards, RG, Sampson, FC, Beard, SM, Tappenden, P. A review of the natural history and epidemiology of multiple sclerosis: implications for resource allocation and health economic models. *Health Technol Assess* 2002; **6**: 1–73.
- Young, PJ, Lederer, C, Eder, K, *et al.* Relapses and subsequent worsening of disability in relapsing-remitting multiple sclerosis. *Neurology* 2006; **67**: 804–808.
- Confavreux, C, Vukusic, S, Moreau, T, Adeleine, P. Relapses and progression of disability in multiple sclerosis. *N Engl J Med* 2000; **343**: 1430–1438.
- Goodin, DS, Frohman, EM, Garmany, GP, *et al.* Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002; **58**: 169–178.
- Rieckmann, P. Multiple Sklerose Therapie Konsensus Gruppe (MSTKG), Immunmodulatorische Stufentherapie der Multiplen Sklerose: Aktuelle Therapieempfehlungen (September 2006). [Escalating immunomodulatory therapy of multiple sclerosis: Update (September 2006).] *Nervenarzt* 2006; **77**: 1506–1518.
- The National Collaborating Centre for Chronic Conditions (NCC-CC). Multiple Sclerosis. National clinical guideline for diagnosis and management in primary and secondary care. Online resource: <http://www.rcplondon.ac.uk/pubs/books/MS/MSfulldocument.pdf>. Royal College of Physicians 2004 [accessed 23.08.07].
- Tremlett, HL, Luscombe, DK, Wiles, CM. Use of corticosteroids in multiple sclerosis by consultant neurologists in the United Kingdom. *J Neurol Neurosurg Psychiatry* 1998; **65**: 362–365.
- Filippini, G, Brusaferrri, F, Sibley, WA, *et al.* Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev* 2000; (4): CD001331.
- Köpke, S, Heesen, C, Kasper, J, Mühlhauser, I. Steroid treatment for relapses in multiple sclerosis – the evidence urges shared decision-making. *Acta Neurol Scand* 2004; **110**: 1–5.
- Sellebjerg, F, Frederiksen, JL, Nielsen, PM, Olesen, J. Double-blind, randomized, placebo-controlled study of oral, high-dose methylprednisolone in attacks of MS. *Neurology* 1998; **51**: 529–534.
- Kasper, J, Köpke, S, Mühlhauser, I, Heesen, C. Evidence-based patient information about treatment of multiple sclerosis—a phase one study on comprehension and emotional responses. *Patient Educ Couns* 2006; **62**: 56–63.
- Whitney, SN, McGuire, AL, McCullough, LB. A typology of shared decision making, informed consent, and simple consent. *Ann Intern Med* 2004; **140**: 54–59.
- Towle, A, Godolphin, W. Framework for teaching and learning informed shared decision making. *BMJ* 1999; **319**: 766–771.
- Heesen, C, Kasper, J, Segal, J, Köpke, S, Mühlhauser, I. Decisional role preferences, risk knowledge and information interests in patients with multiple sclerosis. *Mult Scler* 2004; **10**: 643–650.
- Vickrey, BG, Shatin, D, Wolf, SM, *et al.* Management of multiple sclerosis across managed care and fee-for-service systems. *Neurology* 2000; **55**: 1341–1349.
- Steckelberg, A, Berger, B, Köpke, S, Heesen, C, Mühlhauser, I. Kriterien für evidenzbasierte Patientinformationen. [Criteria for evidence-based patient information] *Z Arztl Fortbild Qualitätssich* 2005; **99**: 343–351.
- Rogers, R. A protection motivation theory of fear appeals and attitude change. *J Psychol* 1975; **91**: 93–114.
- Boer, H, Seydel, ER. Protection motivation theory. In: Connor, M, Norman, P, (eds), *Predicting health behavior*. Buckingham: Open University Press; 1996; **20**: 95–120.
- Meyer, H. *Unterrichtsmethoden* [Teaching methods]. Frankfurt: Cornelsen Scriptor; 1983.
- Köpke, S. Entwicklung eines Schulungsprogramms und Evaluationskonzepts zur Kortisonbehandlung im akuten Schub der Multiplen Sklerose [Development of an educational programme and evaluation concept for corticoid treatment in acute relapses of multiple sclerosis]. Hamburg: University of Hamburg; 2003 (state examination thesis).
- Entwistle, VA, Skea, ZC, O'Donnell, MT. Decisions about treatment: interpretations of two measures of control by women having a hysterectomy. *Soc Sci Med* 2001; **53**: 721–732.
- Gold, SM, Heesen, C, Schulz, H, *et al.* Disease specific quality of life instruments in multiple sclerosis: Validation of the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS). *Mult Scler* 2001; **7**: 119–130.
- Sharrack, B, Hughes, RA. The Guy's Neurological Disability Scale (GNDS): a new disability measure for multiple sclerosis. *Mult Scler* 1999; **5**: 223–233.
- Heesen, C, Reich, C, Borchers, C, Gold, SM, Schulz, KH. Patientenbasierte Scoringssysteme bei Multipler Sklerose – Untersuchung zur Validierung der United Kingdom Disability Scale (UNDS) und des Patient-Generated-Index (PGI). [Patient based scoring instruments in multiple sclerosis – German validation of the United Kingdom Disability Scale (UNDS) and the Patient-Generated-Index (PGI)] *Neurol Rehabil* 2007; **13**: 17–29.
- Newcombe, RG. Improved confidence intervals for the difference between binomial proportions based on paired data. *Stat Med* 1998; **17**: 2635–2650.
- Mohr, DC, Hart, SL, Julian, L, Cox, D, Pelletier, D. Association between stressful life events and exacerbation in multiple sclerosis: a meta-analysis. *BMJ* 2004; **328**: 731–733.
- Campbell, M, Fitzpatrick, R, Haines, A, *et al.* Framework for design and evaluation of complex interventions to improve health. *BMJ* 2000; **321**: 694–696.
- Lenz, M, Steckelberg, A, Richter, B, Mühlhauser, I. Meta-analysis does not allow appraisal of complex interventions in diabetes and hypertension self-management: a methodological review. *Diabetologia* 2007; **50**: 1375–1383.
- Bekker, H, Thornton, JG, Airey, CM, *et al.* Informed decision making: an annotated bibliography and systematic review. *Health Technol Assess* 1999; **3**: 1–156.
- Kasper, J, Burisch, G, Geiger, F, Heesen, C. Do patients perceive the involvement we observe? (abstract). In: Härter, M, Simon, D, Loh, A (eds), 4th International Shared Decision Making Conference. Lengerich: Pabst; 2007; **32**: 147.
- Elwyn, G, O'Connor, A, Stacey, D, *et al.* Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. *BMJ* 2006; **333**: 417–419.
- Newman, S, Steed, L, Mulligan, K. Self-management interventions for chronic illness. *Lancet* 2004; **364**: 1523–1537.